A problem addressed by the presently claimed invention is the instability of the HiB valence. Each of Gold *et al.* and Petre *et al.* circumvent the instability of the HiB valence by extemporaneous addition of it to the vaccine just prior to vaccine administration – Gold *et al.* teaches use of lyophilized HiB valence (p. 349, 1st col., last full paragraph) and Petre *et al.* is silent on the other than to say HiB antigen is "used extemporaneously by formulating the vaccine just prior to administration" (p. 4, lns. 18-19). Neither provide any motivation to modify either of the methods disclosed therein at all, let alone in a manner leading to the presently claimed method. That is, neither suggest separately (a) adsorbing the tetanus toxoid or diphtheria toxoid onto an aluminum salt and (b) preparing the HiB conjugate in a phosphate buffer, and then mixing each with the other components.

Neither do either of Gold *et al.* or Petre *et al.* provide any teachings of a reasonable expectation of success. The Examples of the present specification establish that vaccines according to the invention do not suffer from the problem of antigenic competition as the composition from seroprotection against the corresponding disease of each antigen in the composition.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned attorney as indicated below.

Respectfully submitted,

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**U.S. APPLICATION 09/508,570**

**Redlin d Version of Amended Claims**

21. (Amended) A method for preparing a stabilized multi-component vaccine comprising at least:

a) pertussis toxoid and filamentous hemagglutinin in purified form,

b) tetanus toxoid,

c) diphtheria toxoid,

d) inactivated polio virus, ~~and~~

e) a conjugate of a carrier molecule selected from tetanus toxoid and diphtheria toxoid and a capsular polysaccharide of *Haemophilus influenzae* type B, and

f) an aluminum salt,

wherein tetanus toxoid and diphtheria toxoid are adsorbed onto ~~an~~ the aluminum salt before being mixed with the other components and the conjugate is prepared in a phosphate buffer solution before being mixed with the other components.

25. (Amended) The method according to claim 21, further comprising adding hepatitis B surface antigen adsorbed onto an aluminum salt before being mixed with the other components.

26. (Amended) The method according to claim ~~23~~21, wherein mixing is conducted in the following order:

a) adsorbing tetanus toxoid and diphtheria onto ~~an aluminum salt~~aluminum hydroxide,

b) adsorbing pertussis toxoid and filamentous hemagglutinin in purified form onto an aluminum salt,

c) mixing the components obtained in a) with those obtained in b),

d) adding inactivated polio virus,

e) adding a phosphate buffer solution of a conjugate of a carrier molecule selected from tetanus toxoid and diphtheria toxoid and a capsular polysaccharide of *Haemophilus influenzae* type B.

27. (Amended) A method according to claim 25 wherein mixing is conducted in the following order:

a) adsorbing tetanus toxoid and diphtheria onto ~~an aluminum salt~~aluminum hydroxide,

b) adsorbing pertussis toxoid and filamentous hemagglutinin in purified form onto an aluminum salt,

c) mixing the components obtained in a) with those obtained in b),

d) adding inactivated poliovirus after c),

e) adding hepatitis B surface antigen previously adsorbed onto an aluminum salt after d),

f) adding a phosphate buffer solution of a conjugate of a carrier molecule selected from tetanus toxoid and diphtheria toxoid and a capsular polysaccharide of *Haemophilus influenzae* type B after e).

34. (Amended) A multi-component vaccine ~~according to claim 10~~ obtained by the method of claim 27, wherein the composition of said vaccine comprises per 0.5 ml dose:

g) 25 µg pertussis toxoid;

h) 25 µg filamentous hemagglutinin;

i) 30 LF diphtheria toxoid;

j) 10 Lf tetanus toxoid;

k) 40 D antigen units poliovirus type 1;

l) 8 D antigen units poliovirus type 2;

m) 32 D antigen units poliovirus type 3;

n) 10 µg Haemophilus influenzae type B polysaccharide covalently bound to 20 µg tetanus toxoid; and

o) 5 µg hepatitis B surface antigen;.

~~j) 20 µMoles phosphates;~~

~~k) 5 µMoles carbonates;~~

~~l) 0.125 ml of 50 mM tris buffer; and~~

~~m) 0.306 mg aluminum salt.~~

36. (Amended) A method for conferring protection in a host against disease caused by *Bordetella pertussis*, *Clostridium tetanii*, *Corynebacterium diphtheriae*, *Haemophilus influenzae*, *Poliovirus* and/or *Hepatitis B virus* using a multi-component vaccine ~~according to claim 30~~obtained by the method of claim 27.

37. (Amended) A method of immunizing a human host against disease caused by infection by *Bordetella pertussis*, *Clostridium tetanii*, *Corynebacterium diphtheriae*, *Haemophilus influenzae*, *Poliovirus*, and/or *Hepatitis B virus*, which method comprises administering to the host a multi-component vaccine ~~according to claim 30~~obtained by the method of claim 27.